

CLAIMS:

1. An isolated nucleic acid sequence, of an alternative splicing variant, selected from the group consisting of:

- (i) the nucleic acid sequence depicted in any one of SEQ ID NO:1 to SEQ ID NO:26;
- (ii) nucleic acid sequences having at least 90% identity with the sequence of (i) with the proviso that each sequence is different than the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing; and
- (iii) fragments of (i) or (ii) of at least 20 b.p., provided that said fragment contains a sequence which is not present, as a continuous stretch of nucleotides, in the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing.

2. An isolated nucleic acid sequence complementary to the nucleic acid sequence of Claim 1.

3. An amino acid sequence selected from the group consisting of:

- (i) an amino acid sequence coded by the isolated nucleic acid sequence of alternative splice variants of Claim 1;

(ii) homologues of the amino acid sequences of (i) in which one or more amino acids has been added, deleted, replaced or chemically modified in the region, or adjacent to the region, where the amino acid sequences differs from the original amino acid sequence, coded by the original nucleic acid sequence from which the variant has been varied by alternative splicing.

4. An amino acid sequence according to Claim 3, as depicted in any one of SEQ ID NO:27 to SEQ ID NO:52.

5. An isolated nucleic acid sequence coding for any one of the amino acid sequences of Claim 3 or 4.

6. A purified antibody which binds specifically to any of the amino acid sequence of Claim 3 or 4.

7. A purified antibody which binds to an amino acid sequence which is present only in the alternative splice variant depicted in the amino acid of Claims 3 or 4, but is not present in the original amino sequence.

8. A purified antibody which binds to an amino acid sequence present in the original amino acid sequence, which amino acid sequence is not present in the amino acid sequence of Claims 3 or 4.

9. An expression vector comprising any one of the nucleic acid sequences of Claim 1 or 5 and control elements for the expression of the nucleic acid sequence in a suitable host.

10. An expression vector comprising any one of the nucleic acid sequences of Claim 2, and control elements for the expression of the nucleic acid sequences in a suitable host.

11. A host cell transfected by the expression vector of Claim 9 or 10.

12. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:

- (i) the expression vector of Claim 9; and
- (ii) any one of the amino acid sequences of Claim 3 or 4.

13. A pharmaceutical composition according to Claim 12, for treatment of diseases which can be ameliorated or cured by raising the level of any one of the amino acid sequences depicted in SEQ ID NO:27 to SEQ ID NO:52.

14. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:

- (i) any one of the nucleic acid sequences of Claim 2;
- (ii) the expression vector of Claim 10; and
- (iii) the purified antibody of Claim 6 or 7.

15. A pharmaceutical composition according to Claim 14, for treatment of diseases which can be ameliorated or cured by decreasing the level of any one of the amino acid sequences depicted in SEQ ID NO:27 to SEQ ID NO:52.

16. A method for detecting a variant nucleic acid sequence in a biological sample, comprising the steps of:

- (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1 or 2; and

- (b) detecting said hybridization complex;

wherein the presence of said hybridization complex correlates with the presence of a variant nucleic acid sequence in the said biological sample.

17. A method for determining the level of variant nucleic acid sequences in a biological sample comprising the steps of:

- (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1 or 2; and

(b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

18. A method for determining the ratio between the level of variant of the nucleic acid sequence in a first biological sample and the level of the original sequence from which the variant has been varied by alternative splicing in a second biological sample comprising:

- (a) determining the level of the variant nucleic acid sequence in the first biological sample according to the method of Claim 17;
- (b) determining the level of the original sequence in the second biological sample; and
- (c) comprising the levels obtained in (a) and (b) to give said ratio.

19. A method according to Claim 18, wherein said first and said second biological samples are the same sample.

20. A method according to any of Claims 16 to 19, wherein the nucleic acid material of said biological sample are mRNA transcripts.

21. A method according to Claim 20, where the nucleic acid sequence is present in a nucleic acid chip.

22. A method for identifying candidate compounds capable of binding to the variant product and modulating its activity, the method comprising:

- (i) providing any one of the amino acid sequences as defined in Claim 3 or 4;
- (ii) contacting a candidate compound with said amino acid sequence;
- (iii) determining the effect of said candidate compound on the biological activity of said protein or polypeptide and selecting those compounds which show a significant effect on said biological activity.

23. A method according to Claim 22, wherein the compound is an activator and the measured effect is increase in the biological activity.

24. A method according to Claim 22, wherein the compound is a deactivator and the effect is decrease in the biological activity.

25. An activator of any one of the amino acid sequences of Claim 3 or 4.

25. A deactivator of any one of the amino acid sequences of Claims 3 or 4.

27. A method for detecting any one of the amino acid sequences of Claim 3 or 4 in a biological sample, comprising the steps of:

- (a) contacting with said biological sample the antibody of Claim 6 or 7, thereby forming an antibody-antigen complex; and
- (b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of the desired amino acid in said biological sample.

28. A method for detecting the level of the amino acid sequence of any one of Claim 3 or 4 in a biological sample, comprising the steps of:

- (a) contacting with said biological sample the antibody of Claim 6 or 7, thereby forming an antibody-antigen complex; and
- (b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the level of said amino acid sequence in the sample.

29. A method for determining the ratio between the level of any one of the amino acid sequences of Claims 3 or 4 present in a first biological sample and the level of the original amino acid sequences from which they were varied by alternative splicing, present in a second biological sample, the method comprising:

- (a) determining the level of the amino acid sequences of Claims 3 or 4 into a first sample by the method of Claim 28;
- (b) determining the level of the original amino acid sequence in the second sample; and
- (c) comparing the level obtained in (a) and (b) to give said ratio.

30. A method according to Claim 29, wherein said first and said second biological samples are the same sample.

31. An isolated nucleic acid sequence comprising SEQ ID NO: 21.

32. An isolated nucleic acid sequence which is complementary to the nucleic acid sequence of claim 31.

33. An amino acid sequence encoded by the isolated nucleic acid sequence of claim 31.

34. The amino acid sequence according to claim 33, wherein said amino acid sequence comprises SEQ ID NO: 33.

35. An isolated nucleic acid sequence coding for the amino acid sequence of Claim 33.



36. A purified antibody which bind specifically to the amino acid sequence of Claim 33.

37. A purified antibody which binds to an amino acid sequence which is present only in the alternative splice variant depicted in the amino acid of Claim 33, but is not present in the original amino acid sequence.

38. An expression vector comprising the nucleic acid sequence of claim 31 and control elements for the expression of the nucleic acid sequence in a suitable host.

39. An expression vector comprising the nucleic acid sequence of claim 32 and control elements for the expression of the nucleic acid sequence in a suitable host.

40. An expression vector comprising any one of the nucleic acid sequences of Claim 32, and control elements for the expression of the nucleic acid sequence in a suitable host.

41. A host cell transfected by the expression vector of claim 38.

42. A host cell transfected by the expression vector of claim 39.

43. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient the expression vector of Claim 36.

44. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient the amino acid sequence of Claim 33.

45. A composition according to claim 44 for the treatment of diseases which can be ameliorated or cured by raising the level of the amino acid sequence depicted in SEQ ID NO: 33.

46. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient the nucleic acid sequence of Claim 32.

47. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient the expression vector of Claim 38.

48. A pharmaceutical composition comprising a pharmaceutically acceptable carrier as an active ingredient the purified antibody of Claim 34.

49. A pharmaceutical composition according to Claim 44 for the treatment of diseases which can be ameliorated

or cured by decreasing the level of the amino acid sequence depicted in SEQ ID NO: 33.

50. A pharmaceutical composition according to Claim 45 for the treatment of diseases which can be ameliorated or cured by decreasing the level of the amino acid sequence depicted in SEQ ID NO: 33.

51. A pharmaceutical composition according to Claim 46 for the treatment of diseases which can be ameliorated or cured by decreasing the level of the amino acid sequence depicted in SEQ ID NO: 33.

52. A method for detecting a variant nucleic acid sequence in a biological sample, comprising:

- (a) hybridizing to nucleic acid material of said biological sample the nucleic acid sequence of Claim 31 or an isolated nucleic acid complementary to the nucleic acid of Claim 31; and
- (b) detecting the hybridization complex; wherein the presence of said hybridization complex correlates with the presence of a variant nucleic acid sequence in the said biological sample.

53. A method for determining the level of variant nucleic acid sequence in a biological sample comprising:

- (a) hybridizing to a nucleic acid material of said biological sample the nucleic acid sequence of Claim 31 or an isolated nucleic acid sequence complementary to the nucleic acid sequence of Claim 31; and
- (b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

54. A method for determining the ratio between the level of variant of the nucleic acid sequence in a first biological sample and the level of the original sequence from which the variant has been varied by alternative splicing in a second biological sample, comprising:

- (a) determining the level of the variant nucleic acid sequence in the first biological sample according to the method of Claim 51;
- (b) determining the level of the original sequence in a second biological sample; and
- (c) comparing the levels obtained in (a) and (b) to give said ratio.

55. A method according to Claim 52, wherein said first and second biological samples are the same sample.

56. A method according to Claim 50, wherein the nucleic acid material of said biological sample are mRNA transcripts.

57. A method according to Claim 51, wherein the nucleic acid material of said biological sample are mRNA transcripts.

58. A method according to Claim 52, wherein the nucleic acid material of said biological sample are mRNA transcripts.

59. A method according to Claim 52, wherein the nucleic acid material of said biological sample are mRNA transcripts.

60. A method according to Claim 52, wherein the nucleic acid sequence is present in a nucleic acid chip.

61. A method according to Claim 53, wherein the nucleic acid sequence is present in a nucleic acid chip.

62. A method according to Claim 53, wherein the nucleic acid sequence is present in a nucleic acid chip.

63. A method according to Claim 53, wherein the nucleic acid sequence is present in a nucleic acid chip.

64. A method for identifying candidate compounds capable of binding to the variant product and modulating its activity, the method comprising:

- (a) providing the amino acid sequence as defined in Claim 33;
- (b) contacting a candidate compound with said amino acid sequence; and
- (c) determining the effect of said candidate compound on the biological activity of said protein or polypeptide and selecting those compounds which show a significant effect on said biological activity.

65. A method according to Claim 55, wherein the compound is an activator and the measured effect is increased in the biological activity.

66. A method according to Claim 55, wherein the compound is a deactivator and effect is decreased in the biological activity.

67. An activator of the amino acid sequence of Claim 33.

68. A deactivator of the amino acid sequence of Claim 33.

69. A method for detecting the amino acid sequence of Claim 33 in a biological sample, comprising:

- (a) contacting with said biological sample the antibody of Claim 34, thereby forming an antibody-antigen complex; and
- (b) detecting said antibody-antigen complex wherein the presence of said antibody-antigen complex correlates with the presence of the desired amino acid in said biological sample.

70. A method for detecting the level of the amino acid sequence of Claim 33 in a biological sample, comprising:

- (a) contacting with same biological sample the antibody of Claim 34, thereby forming an antibody-antigen complex; and
- (b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the level of said amino acid sequence in the sample.

71. A method for determining the ratio between the level of the amino acid sequence of Claim 33 present in a first biological sample and the level of the original amino acid sequence from which they were varied by alternative splicing, present in a second biological sample, the method comprising:

- (a) determining the level of the amino acid sequence of Claim 33 into a first sample by the method of Claim 61;
- (b) determining the level of the original amino acid sequence in the second sample; and
- (c) comparing the level obtained in (a) and (b) to give said ratio.

72. A method according to Claim 62, wherein said first and said second biological samples are the same samples.

73. An expression vector comprising a nucleic acid which is complementary to an isolated nucleic acid consisting essentially of exons 1-5 and 7-9 of a nucleotide sequence encoding CD40, and control elements for the expression of the nucleic acid in a suitable host.

74. A host cell transfected by the expression vector of claim 73.

75. A composition comprising a pharmaceutically acceptable carrier and as an active ingredient the expression vector of claim 73.

76. A composition comprising a pharmaceutically acceptable carrier and as an active ingredient the



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expression vector of claim 39.